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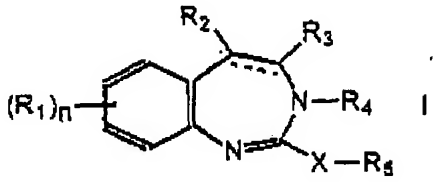
Cet (08.20.04)

Claim 1 (Original)

1. Benzodiazepine derivative of formula I:



I

in which

the dashed lines indicate the possible presence of a double bond;

R_1 represents optionally halogenated (C_1-C_{18})alkyl, optionally halogenated (C_1-C_{18})alkoxy, halogen, nitro, hydroxyl or (C_6-C_{18})aryl (optionally substituted with optionally halogenated (C_1-C_{10})alkyl, optionally halogenated (C_1-C_{12})alkoxy, halogen, nitro or hydroxyl);

n represents 0, 1, 2, 3 or 4;

R_2 and R_3 represent, independently of each other, hydrogen; optionally halogenated (C_1-C_{18})alkyl; (C_1-C_{18})alkoxy; (C_6-C_{18})aryl; (C_6-C_{18})aryl(C_1-C_{12})alkyl; heteroaryl; heteroaryl(C_1-C_{12})alkyl; (C_6-C_{18})aryloxy; (C_6-C_{18})aryl(C_1-C_{12})alkoxy; heteroaryloxy; or heteroaryl(C_1-C_{12})alkoxy; in which the aryl and heteroaryl portions of these radicals are optionally substituted with halogen, optionally halogenated (C_1-C_{12})alkoxy, optionally halogenated (C_1-C_{12})alkyl, nitro and hydroxyl;

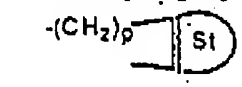
R_4 represents hydrogen, (C_1-C_{18})alkyl or (C_6-C_{18})aryl, the said aryl group optionally being substituted with halogen, optionally halogenated (C_1-C_{12})alkoxy, optionally halogenated (C_1-C_{12})alkyl, nitro or hydroxyl;

X represents S, O or -NT in which T represents a hydrogen atom, (C_1-C_{12})alkyl, (C_6-C_{18})aryl, (C_6-C_{18})aryl(C_1-C_{12})alkyl or (C_6-C_{18})arylcarbonyl;

R_3 represents (C_1-C_{18})alkyl; hydroxy(C_1-C_{18})alkyl; (C_6-C_{18})aryl(C_1-C_{12})alkyl; (C_3-C_{12})cycloalkyl(C_1-C_{12})alkyl; (C_3-C_{12})cycloalkenyl-(C_1-C_{12})alkyl; heteroaryl(C_1-C_{12})alkyl optionally substituted with one or more substituents Su as defined below; (C_3-C_{12})cycloalkyl optionally substituted with oxo and optionally fused to (C_6-C_{18})aryl, the assembly optionally being substituted with one or more substituents Su as defined below; a group $-CH_2-CR_a=CR_bR_c$ (in which R_a, R_b and R_c are chosen, independently, from (C_1-C_{18})alkyl, (C_2-C_{18})alkenyl, hydrogen and (C_6-C_{18})aryl); a group -CHA-CO-Z (in which Z represents optionally halogenated (C_1-C_{18})alkyl; optionally halogenated (C_1-C_{18})alkoxy; (C_3-C_{12})cycloalkyl; (C_3-C_{12})cycloalkyl optionally substituted with oxo and optionally fused to (C_6-C_{18})aryl; (C_6-C_{18})aryl(C_1-C_{18})alkyl; (C_6-C_{18})aryl(C_1-C_{12})-alkoxycarbonylamino(C_1-C_{12})alkyl in which alkyl is optionally substituted with (C_1-C_{12})alkoxycarbonyl(C_1-C_{12})alkyl; (C_1-C_{12})alkoxy-carbonyl; (C_1-C_{12})alkoxycarbonyl(C_1-C_{12})alkyl; (C_6-C_{10})aryl; (C_6-C_{18})aryl fused to an unsaturated heterocycle optionally substituted with oxo; or heteroaryl;

the aryl, heterocycle, cycloalkyl and heteroaryl portions of these radicals optionally being substituted with halogen; hydroxyl; optionally halogenated (C_1-C_{12})alkyl; optionally halogenated (C_1-C_{12})alkoxy; nitro; cyano; (C_1-C_{12})alkylenedioxy; (C_1-C_{12})alkylene; carboxy(C_1-C_{12})alkyl; (C_2-C_{12})alkenyloxy; optionally halogenated (C_1-C_{12})alkylsulphonyloxy; cyano(C_1-C_{12})-alkyl; -Cy-alk-NH-SO_2-Ar in which alk represents (C_1-C_{12})alkyl, Cy represents (C_3-C_{12})cycloalkyl optionally substituted with one or more substituents Su as defined below and Ar represents (C_6-C_{18})aryl optionally substituted with one or more substituents Su as defined below; -alk-Cy in which alk and Cy are as defined above; (C_1-C_{12})alkoxycarbonyl(C_1-C_{12})alkoxy; (C_1-C_{12})alkoxycarbonyl(C_1-C_{12})alkyl; saturated hetero-

cycle optionally substituted with one or more substituents Su as defined below; (C_1-C_{12})alkylcarbonyloxy; (C_1-C_{12})alkylcarbonylamino; optionally halogenated (C_1-C_{12})alkylthio; (C_1-C_{12})alkylcarbonyloxy(C_1-C_{12})alkoxy; a group of formula:



in which p = 0, 1, 2, 3 or 4 and in which St is (C_6-C_{18})aryl optionally substituted with one or more substituents Su as defined below; (C_1-C_{12})alkoxycarbonyl; (C_6-C_{18})arylthio optionally substituted with one or more substituents Su as defined below; (C_3-C_{12})cycloalkyl optionally substituted with one or more substituents Su as defined below; -Cy-CO-O-alk in which alk and Cy are as defined above; -alk-Cy-alk'-NH-CO-alk" in which alk and Cy are as defined above, alk' and alk" represent, independently of each other, (C_1-C_{12})alkyl; $-NR^o-CO-alk'$-Het in which alk' is as defined above, R^o represents H or (C_1-C_{12})alkyl and Het represents heteroaryl optionally substituted with one or more substituents Su as defined below; di(C_1-C_{12})alkoxyphosphoryl(C_1-C_{12})alkyl; or (C_6-C_{18})aryl optionally substituted with one or more substituents Su as defined below; (C_6-C_{18})aryloxy optionally substituted with one or more substituents Su as defined below; (C_6-C_{18})aryl fused to an unsaturated heterocycle optionally substituted on the heterocycle portion with oxo, the assembly optionally being substituted with one or more substituents Su as defined below; (C_6-C_{18})aryl(C_1-C_{12})alkoxy optionally substituted with one or more substituents Su as defined below; (C_6-C_{18})arylsulphonyl optionally substituted with one or more substituents Su as defined below; (C_6-C_{18})aryl(C_1-C_{12})alkyl in which aryl is optionally substituted with one or more substituents Su as defined below; (C_6-C_{18})arylcarbonyl optionally substituted with one or more substituents Su as defined below; and

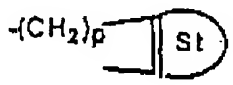
A represents a hydrogen atom, a (C_6-C_{18})aryl group optionally substituted with one or more substituents Su or (C_1-C_{12})alkyl};

or alternatively R_4 and R_5 together form a group $-CR_6=CR_7-$ in which CR_6 is linked to X and in which:

R_6 represents a hydrogen atom; (C_1-C_{18})alkyl; (C_3-C_{12})cycloalkyl; (C_6-C_{18})aryl; carboxy(C_1-C_{12})alkyl; (C_1-C_{12})alkoxycarbonyl(C_1-C_{12})alkyl; heteroaryl; (C_6-C_{18})aryl(C_1-C_{12})alkyl; and heteroaryl(C_1-C_{12})alkyl; in which the aryl and heteroaryl portions of these radicals are optionally substituted with (C_1-C_{12})alkyl, (C_1-C_{12})alkoxy, hydroxyl, nitro, halogen or di(C_1-C_{12})alkoxyphosphoryl(C_1-C_{12})alkyl;

R_7 represents a hydrogen atom; hydroxyl; di(C_1-C_{12})alkylamino(C_1-C_{12})alkyl; optionally halogenated (C_1-C_{18})alkyl; carboxyl; carboxy(C_1-C_{12})alkyl optionally substituted with amino; (C_1-C_{12})alkoxycarbonyl; (C_6-C_{18})aryl; heteroaryl; (C_6-C_{18})aryl(C_1-C_{12})alkyl; or heteroaryl(C_1-C_{12})alkyl; (C_6-C_{18})aryl fused to an unsaturated heterocycle, optionally substituted on the heterocycle portion with oxo; (C_3-C_{12})cycloalkyl;

in which the aryl, heterocycle, cycloalkyl and heteroaryl portions of these radicals are optionally substituted with halogen; hydroxyl; hydroxy(C_1-C_{12})alkoxy; optionally halogenated (C_1-C_{12})alkyl; optionally halogenated (C_1-C_{12})alkoxy; carboxyl; (C_1-C_{12})alkoxycarbonyl; nitro; cyano; cyano(C_1-C_{18})alkyl; (C_1-C_{18})alkylcarbonyloxy; (C_2-C_{12})alkylene; (C_1-C_{12})alkylenedioxy; (C_1-C_{12})alkylthio; (C_6-C_{18})arylthio optionally substituted with one or more substituents Su as defined above; di(C_1-C_{12})alkylamino; a group of formula:



in which p = 0, 1, 2, 3 or 4 and in which St represents (C_6-C_{18})aryl; -alk-Cy-NH-SO_2-Ar in which alk

represents (C_1-C_{12})alkyl, Cy represents (C_3-C_{12})cycloalkyl optionally substituted with one or more substituents Su as defined below and Ar represents (C_6-C_{18})aryl optionally substituted with one or more substituents Su as defined below; -Cy-alk-NH-SO_2-Ar in which Cy, alk and Ar are as defined above; -alk-Cy in which alk and Cy are as defined above; -alk-Cy-alk'-NH-CO-alk" in which alk and Cy are as defined above and alk' and alk" represent, independently, (C_1-C_{12})alkyl; di(C_1-C_{12})alkoxyphosphoryl(C_1-C_{12})alkyl; (C_6-C_{18})aryl optionally substituted with one or more substituents Su as defined below; (C_6-C_{18})aryloxy optionally substituted with one or more substituents Su as defined below; (C_6-C_{18})arylcarbonyl optionally substituted with one or more substituents Su as defined below; (C_6-C_{18})arylsulphonyl optionally substituted with one or more substituents Su as defined below; (C_6-C_{18})aryl(C_1-C_{12})alkoxy in which the aryl portion is optionally substituted with one or more substituents Su as defined below; saturated heterocycle optionally substituted with one or more substituents Su as defined below; (C_6-C_{18})aryl(C_1-C_{12})alkyl optionally substituted with one or more substituents Su as defined below;

Su is chosen from hydroxyl, halogen, cyano, nitro, optionally halogenated (C_1-C_{12})alkyl and optionally halogenated (C_1-C_{12})alkoxy;

or alternatively R_6 and R_7 together form a C_3-C_{12} alkylene chain optionally interrupted with a nitrogen atom which is optionally substituted with (C_1-C_{12})alkyl or (C_6-C_{18})aryl or (C_6-C_{18})aryl(C_1-C_{12})alkyl, the ring formed by $CR_6=CR_7$ optionally being fused to (C_6-C_{18})aryl (the aryl portions of these radicals optionally being substituted with halogen, nitro, hydroxyl, optionally halogenated (C_1-C_{12})alkyl or optionally halogenated (C_1-C_{12})alkoxy);

with the exclusion of the compounds of formula I in which X = S; n = 0; R_2 represents methyl and R_3 represents a hydrogen atom; R_4 and R_5 together form a group -$CR_6=CR_7$- in which CR_6 is linked to X, R_6 and R_7 together form a -$(CH_2)_3$- or -$(CH_2)_4$- chain or alternatively R_6 represents a hydrogen atom or a propyl group and R_7 is a phenyl group optionally substituted with -OCH_3 or a hydroxyl group;

and the pharmaceutically acceptable salts thereof with acids or bases.

Claim 2 (Original)

2. Compound according to Claim 1, characterized in that X represents -NT in which T is as defined in Claim 1 and R_4 and R_5 together form $-CR_6=CR_7$.

3. (Amended) Compound according to Claim 1, characterized in that R_3 represents a hydrogen atom.

4. (Amended) Compound according to Claim 1, characterized in that R_2 represents a hydrogen atom or a (C_6-C_{10}) aryl group optionally substituted with halogen, (C_1-C_6) alkoxy, optionally halogenated (C_1-C_6) alkyl, nitro and hydroxyl.

5. (Amended) Compound according to Claim 1, characterized in that n is 0 or 1 and R_1 represents a halogen atom.

6. (Amended) Compound according to Claim 1, characterized in that X represents S;

R_4 represents a hydrogen atom;

R_5 represents (C_1-C_6)alkyl; hydroxy(C_1-C_6)alkyl; (C_6-C_{10})aryl(C_1-C_6)alkyl; (C_5-C_8)cycloalkenyl(C_1-C_6)alkyl; or isoxazolyl(C_1-C_6)alkyl optionally substituted with one or more (C_1-C_6)alkyls; $-CH_2-CR_a=CR_bR_c$ in which R_a is a hydrogen atom, (C_1-C_6)alkyl or (C_6-C_{10})aryl, R_b is (C_1-C_6)alkyl or a hydrogen atom and R_c represents a hydrogen atom or (C_2-C_{10})alkenyl; a group $-CH_2-CO-Z$ in which Z represents (C_1-C_{10})alkyl, (C_6-C_{10})aryl(C_1-C_6)alkyl, 5- or 6-membered heteroaryl or (C_6-C_{10})aryl optionally fused to a 5- to 7-membered aromatic or unsaturated heterocycle; the aryl and heteroaryl portions of these radicals optionally being substituted with halogen, hydroxyl, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, nitro or (C_6-C_{10})aryl (optionally substituted with halogen, optionally halogenated (C_1-C_6)alkyl, optionally halogenated (C_1-C_6)alkoxy or nitro);

or alternatively R_4 and R_5 together form a group $-CR_6=CR_7-$ in which

R_6 represents a hydrogen atom, (C_1-C_6)alkyl, (C_6-C_{10})aryl (optionally substituted with halogen, hydroxyl, nitro, (C_1-C_6)alkyl or (C_1-C_6)alkoxy), carboxy(C_1-C_6)alkyl, or (C_1-C_6)alkoxy-carbonyl(C_1-C_6)alkyl; and

R_7 represents a hydrogen atom; hydroxyl; di(C_1-C_6)alkylamino(C_1-C_6)alkyl; (C_1-C_{10})alkyl; (C_1-C_6)alkoxycarbonyl; (C_6-C_{10})aryl; heteroaryl; (C_6-C_{10})aryl(C_1-C_6)alkyl; the aryl and heteroaryl portions of these radicals optionally being substituted with (C_1-C_6)alkoxycarbonyl, halogen, hydroxyl, (C_1-C_6)alkyl; (C_6-C_{10})aryl, (this radical optionally being substituted with halogen, optionally halogenated (C_1-C_6)alkyl, (C_1-C_6)alkoxy or nitro) or (C_6-C_{10})aryl fused to a 5- to 7-membered aromatic or unsaturated heterocycle comprising one, two or three endocyclic hetero atoms chosen from O, N and S; or alternatively R_6 and R_7 together form an alkylene chain interrupted with a nitrogen atom optionally substituted with (C_6-C_{10})aryl(C_1-C_6)alkyl in which the aryl portion is optionally substituted with halogen, optionally halogenated (C_1-C_6)alkyl, (C_1-C_6)alkoxy, hydroxyl or nitro.

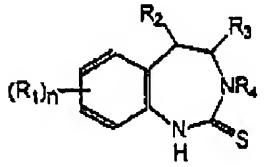
7. (Amended) Compound according to Claim 1, characterized in that X represents -NT; and R_4 and R_5 together form a group $-CR_6=CR_7-$ in which R_6 represents a hydrogen atom and R_7 represents hydroxyl or (C_6-C_{10}) aryl optionally substituted with halogen , nitro, hydroxyl, optionally halogenated (C_1-C_6) alkyl or (C_1-C_6) alkoxy.

Claim 8 (Original)

8. Compound according to Claim 1, chosen from:
3-(biphenyl-4-yl)-5,6-dihydrothiazolo[2,3-b]-1,3-benzodiazepine;
3-(2-furyl)-5,6-dihydrothiazolo[2,3-b]-1,3-benzodiazepine;
3-[4-(ethoxycarbonyl)phenyl]-5,6-dihydro-thiazolo-(2,3-b]-1,3-benzodiazepine;
1-(2-furyl)-2-(4,5-dihydro-3*H*-1,3-benzodiazepine-2-ylsulphamyl)ethanone;
1-(biphenyl-4-yl)-2-(4,5-dihydro-3*H*-1,3-benzo-diazepine-2-ylsulphamyl)ethanone;
3-(biphenyl-3-yl)-5,6-dihydrothiazolo[2,3-b]-1,3-benzodiazepine;
1-(3,4-dihydroxyphenyl)-2-(4,5-dihydro-3*H*-1,3-benzodiazepine-2-ylsulphamyl)ethanone;
3-(3,4-dihydroxyphenyl)-5,6-dihydro-thiazolo[2,3-b]-1,3-benzodiazepine; and
3-(biphenyl-4-yl)-7-chloro-5,6-dihydro-thiazolo[2,3-b]-1,3-benzodiazepine.

Claim 9 (Original)

9. Process for preparing a compound of formula I according to Claim 1, in which X represents S; and R_4 and R_5 do not together form $-CR_6=CR_7-$, comprising the reaction of a thione of formula II:



II

in which:

R_1, n, R_2, R_3 and R_4 are as defined in Claim 1, with a halo derivative of formula III:

$$Hal^1-R_5 \qquad III$$

in which R_5 is as defined in Claim 1 and Hal^1 is a halogen atom, optionally halogenated (C_1-C_6)alkylsulphonyl or (C_6-C_{10})arylsulphonyl optionally substituted in the aryl portion with (C_1-C_6)alkyl.

Claim 10 (Original)

10. Process according to Claim 9, characterized in that the thione of formula II is reacted with an α-halo ketone of formula IVa:

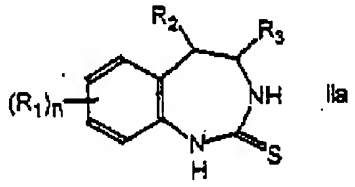
$$Z-CO-CH_2-Hal^2 \qquad IVa$$

in which Z is as defined in Claim 1 and Hal^2 is a halogen atom, so as to obtain the corresponding compounds of formula I in which R_5 represents $-CH_2-CO-Z$.

11. (Amended) Process according to Claim 9, also comprising the alkylation of a compound of formula I obtained according to the process of Claim 9 or Claim 10 in which R_4 represents a hydrogen atom using a suitable alkylating agent, so as to obtain the corresponding compound of formula I in which R_4 represents (C_1-C_{18}) alkyl.

Claim 12 (Original)

12. Process for preparing compounds of formula I according to Claim 1, in which X represents S and R_4 and R_5 together form a group $-CR_6=CR_7-$, comprising the reaction of a thione of formula IIa:



IIa

in which n, R_1, R_2 and R_3 are as defined in Claim 1, with an α-halo ketone of formula IVb:

$$R_7\text{-}CO\text{-}CHR_6\text{-}Hal^3 \qquad \text{IVb}$$

in which R_6 and R_7 are as defined in Claim 1, and Hal^3 represents a halogen atom, in a C_2-C_5 aliphatic carboxylic acid, at a temperature of between 90 and 130°C.

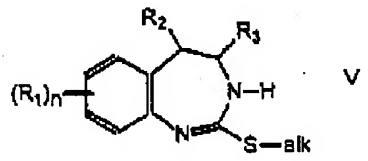
Claim 13 (Original)

13. Process according to Claim 12, characterized in that the aliphatic carboxylic acid is acetic acid.

14. (Amended) Process according to Claim 12, characterized in that the temperature is maintained at between 100 and 125 °C.

Claim 15 (Original)

15. Process for preparing compounds of formula I according to Claim 1, in which X represents -NH, R_4 and R_5 together form a group $-CR_6=CR_7-$ and R_7 is not hydroxyl, comprising the reaction of a sulphide of formula V:



V

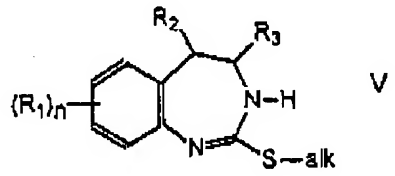
in which n, R_1, R_2 and R_3 are as defined in Claim 1, R_4 and R_5 together form a $-CR_6=CR_7-$ group and alk represents (C_1-C_6)alkyl, with a protected derivative of the ketone of formula VI:

$$NH_2-CHR_6-CO-R_7 \qquad \text{VI}$$

in which the carbonyl group is protected with a protecting group that is labile in acidic medium, R_6 and R_7 being as defined in Claim 1, followed by treatment of the resulting compound with an acid.

Claim 16 (Original)

16. Process for preparing compounds of formula I according to Claim 1, in which X represents -NT in which T is not a hydrogen atom, R_4 and R_5 together form a group $-CR_6=CR_7$, and R_7 represents hydroxyl, comprising the reaction of a sulphide of formula V:



V

in which n, R_1, R_2 and R_3 are as defined in Claim 1, and alk represents (C_1-C_6)alkyl,

with a derivative of formula VIII:

$$HTN-CHR_6-CO-Y \qquad VIII$$

in which T and R_6 are as defined in Claim 1 and Y is a leaving group, at a temperature of between 50 and 150°C and preferably at a temperature of between 60 and 100°C.

17. Process according to Claim 15, also comprising the reaction of the compound obtained by carrying out the process of Claim 15, with a halogenated reagent of formula Hal-T in which T represents (C_1-C_6)alkyl, (C_6-C_{10})aryl or (C_6-C_{10})aryl(C_1-C_6)alkyl and Hal is a halogen atom, in the presence of a base, so as to synthesize the corresponding compound of formula I in which T represents (C_1-C_6)alkyl, (C_6-C_{10})aryl or (C_6-C_{10})aryl(C_1-C_6)alkyl.

Claim 17 (Original)

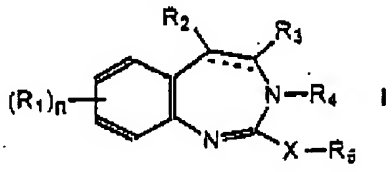
17. Process according to Claim 15, also comprising the reaction of the compound obtained by carrying out the process of Claim 15, with a halogenated reagent of formula Hal-T in which T represents (C_1-C_6)alkyl, (C_6-C_{10})aryl or (C_6-C_{10})aryl(C_1-C_6)alkyl and Hal is a halogen atom, in the presence of a base, so as to synthesize the corresponding compound of formula I in which T represents (C_1-C_6)alkyl, (C_6-C_{10})aryl or (C_6-C_{10})aryl(C_1-C_6)alkyl.

18. (Amended) Pharmaceutical composition containing an effective amount of at least one compound of formula (I) according to Claim 1, in combination with at least one pharmaceutically acceptable vehicle.

19. (Amended) Use of a compound of formula I according to Claim 1, for the preparation of a medicinal product for preventing or treating dyslipidaemia, atherosclerosis and diabetes and its complications.

Claim 20 (Original)

20. Benzodiazepine derivative of formula I:



I

in which

the dashed lines indicate the possible presence of a double bond;

R_1 represents optionally halogenated (C_1-C_{18})alkyl, optionally halogenated (C_1-C_{18})alkoxy,

halogen, nitro, hydroxyl or (C_6-C_{10})aryl (optionally substituted with optionally halogenated (C_1-C_6)alkyl, optionally halogenated (C_1-C_6)alkoxy, halogen, nitro or hydroxyl);

n represents 0, 1, 2, 3 or 4;

R_2 and R_3 represent, independently of each other, hydrogen; optionally halogenated (C_1-C_{18})alkyl; (C_1-C_{18})alkoxy; (C_6-C_{10})aryl; (C_6-C_{10})aryl(C_1-C_6)alkyl; heteroaryl; heteroaryl(C_1-C_6)alkyl; (C_6-C_{10})aryloxy; (C_6-C_{10})aryl(C_1-C_6)alkoxy; heteroaryloxy; or heteroaryl(C_1-C_6)alkoxy; in which heteroaryl represents a 5- to 7-membered aromatic heterocycle containing one, two or three endocyclic hetero atoms chosen from O, N and S, and in which the aryl and heteroaryl portions of these radicals are optionally substituted with halogen, optionally halogenated (C_1-C_6)alkoxy, optionally halogenated (C_1-C_6)alkyl, nitro and hydroxyl;

R_4 represents hydrogen, (C_1-C_{18})alkyl or (C_6-C_{10})aryl, the said aryl group optionally being substituted with halogen, optionally halogenated (C_1-C_6)alkoxy, optionally halogenated (C_1-C_6)alkyl, nitro or hydroxyl;

X represents S, O or -NT in which T represents a hydrogen atom, (C_1-C_6)alkyl, (C_6-C_{10})aryl, (C_6-C_{18})aryl(C_1-C_6)alkyl or (C_6-C_{10})arylcarbonyl;

R_5 represents (C_1-C_{18})alkyl; hydroxy(C_1-C_{18})alkyl; (C_6-C_{10})aryl(C_1-C_6)alkyl; (C_3-C_8)cycloalkyl(C_1-C_6)alkyl; (C_3-C_8)cycloalkenyl-(C_1-C_6)alkyl; isoxazolyl(C_1-C_6)alkyl optionally substituted with (C_1-C_6)alkyl; a group $-CH_2-CR_aR_b=CR_bR_c$ in which R_a, R_b and R_c are chosen independently from (C_1-C_{18})alkyl, (C_2-C_{18})alkenyl, hydrogen and (C_6-C_{10})aryl; a group $-CH_2-CO-Z$ in which Z represents (C_1-C_{18})alkyl, (C_1-C_6)alkoxycarbonyl, (C_6-C_{10})aryl(C_1-C_6)alkyl, (C_6-C_{10})aryl optionally fused to a 5- to 7-membered aromatic or unsaturated heterocycle comprising one, two or three endocyclic hetero atoms chosen from O, N and S; or 5- to 7-membered heteroaryl containing one, two or three endocyclic hetero atoms chosen from O, N and

8; the aryl and heteroaryl portions of these radicals optionally being substituted with halogen, hydroxyl, optionally halogenated (C_1-C_6)alkyl, optionally halogenated (C_1-C_6)alkoxy, nitro, di(C_1-C_6)alkoxyphosphoryl(C_1-C_6)alkyl or (C_6-C_{10})aryl (optionally substituted with halogen, optionally halogenated (C_1-C_6)alkyl, optionally halogenated (C_1-C_6)alkoxy, nitro or hydroxyl);

or alternatively R_4 and R_5 together form a group $-CR_6=CR_7-$ in which CR_6 is linked to X and in which:

R_6 represents a hydrogen atom; (C_1-C_{18})alkyl; (C_3-C_8)cycloalkyl; (C_6-C_{10})aryl; carboxy(C_1-C_6)alkyl; (C_1-C_6)alkoxycarbonyl(C_1-C_6)alkyl; heteroaryl; (C_1-C_6)aryl(C_1-C_6)alkyl; and heteroaryl(C_1-C_6)alkyl; in which heteroaryl represents a 5- to 7-membered aromatic heterocycle containing one, two or three endocyclic hetero atoms chosen from O, N and S and in which the aryl and heteroaryl portions of these radicals are optionally substituted with (C_1-C_6)alkyl, (C_1-C_6)alkoxy, hydroxyl, nitro, halogen or di(C_1-C_6)alkoxyphosphoryl(C_1-C_6)alkyl;

R_7 represents a hydrogen atom; hydroxyl; di(C_1-C_6)alkylamino(C_1-C_6)alkyl; (C_1-C_{18})alkyl; carboxyl; (C_1-C_6)alkoxycarbonyl; (C_6-C_{10})aryl; heteroaryl; (C_6-C_{10})aryl(C_1-C_8)alkyl; or heteroaryl(C_1-C_6)alkyl; in which heteroaryl represents a 5- to 7-membered aromatic heterocycle containing one, two or three endocyclic hetero atoms chosen from O, N and S and in which the aryl and heteroaryl portions of these radicals are optionally substituted with halogen, hydroxyl, optionally halogenated (C_1-C_6)alkyl, optionally halogenated (C_1-C_6)alkoxy, carboxyl, (C_1-C_6)alkoxycarbonyl, nitro, di(C_1-C_6)alkoxyphosphoryl(C_1-C_6)alkyl, or (C_6-C_{10})aryl (this radical optionally being substituted with hydroxyl, nitro, optionally halogenated (C_1-C_6)alkyl, optionally halogenated (C_1-C_6)alkoxy or halogen) or (C_6-C_{10})aryl fused to a 5- to 7-membered aromatic or unsaturated heterocycle

comprising one, two or three endocyclic hetero atoms chosen from O, N and S;

or alternatively R_6 and R_7 together form a C_3-C_6 alkylene chain optionally interrupted with a nitrogen atom which is optionally substituted with (C_1-C_6)alkyl, or (C_6-C_{10})aryl or (C_6-C_{10})aryl(C_1-C_6)alkyl, (the aryl portions of these radicals optionally being substituted with halogen, nitro, hydroxyl, optionally halogenated (C_1-C_6)alkyl or optionally halogenated (C_1-C_6)alkoxy);

with the exclusion of the compounds of formula I in which X = S; n = 0; R_2 represents methyl and R_3 represents a hydrogen atom; R_4 and R_5 together form a group $-CR_6=CR_7-$ in which CR_6 is linked to X, R_6 and R_7 together form a $-(CH_2)_3-$ or $-(CH_2)_4-$ chain or alternatively R_6 represents a hydrogen atom or a propyl group and R_7 is a phenyl group optionally substituted with $-OCH_3$ or a hydroxyl group;

and the pharmaceutically acceptable salts thereof with acids or bases.